

RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 2, and 4-10 are currently pending and under consideration in the case and are presented herein for reconsideration.

B. Rejection Under 35 U.S.C. §103

The Action maintains the rejection of claims 1, 2, 4-10 and 13 as obvious under 35 U.S.C. § 103(a) over Rhodes (U.S. Patent No. 5,710,368) in view of Russell *et al.* (EPO 0430511A1) in view of Botterman *et al.* (*Herbic. Resist. Weeds Crops* 1991). In particular, it is stated that the Rhodes patent teaches soybean seeds and plants with resistance to glyphosate and contain the ALS gene that retain a commercially acceptable yield. It is asserted that Botterman teaches soybean plants tolerant to glufosinate, and that it would have been obvious to cross a plant according to Rhodes having glyphosate tolerance to a plant of Botterman to arrive at the claimed invention.

1. **Rhodes is Commonly Owned and Cannot Be Used As Prior Art**

Applicants initially note that the Rhodes patent is subject to an obligation of assignment to Asgrow Seed Company as shown at Reel/Frame 007997/0135. The current case is also assigned to the Asgrow Seed Company as evidenced at Reel/Frame 008557/0903.

Although the Action states that the Rhodes patent is prior art under 35 U.S.C. § 102(a), it is actually prior art under §102(e). According to MPEP § 706.02(a)(C), “[f]or 35 U.S.C. § 102(a) to apply, the reference must have a publication date earlier in time than the effective filing date of the application.” The current application claims priority to SN 08/813,788 filed March 7, 1997, now U.S. Patent 6,376,754. This effective filing date is prior to the January 20, 1998

publication date of Rhodes, and therefore the Rhodes patent must be cited as § 102(e) prior art.

Pursuant to 35 U.S.C. § 103(c), subject matter that is:

developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

As both the Rhodes patent and the current case were subject to a common obligation of assignment to Asgrow Seed Company as of the priority date as evidenced by the above-referenced recorded assignments, the Rhodes patent may not be cited as prior art against the current case. Given that the entire Action is premised on the teaching of the Rhodes patent, the rejection is moot and Applicants thus respectfully request withdrawal of the rejection.

2. The Patentability of the Claimed Invention Over the Cited Subject Matter Has Been Acknowledged on the Record

In order to support the rejection it has been asserted that the claimed plants having tolerance to glyphosate and glufosinate are obvious in view of the alleged teaching in the prior art of plants with two herbicide tolerances generally, or with tolerance to glyphosate and sulfonylurea according to Rhodes *et al.* However, the Restriction Requirement mailed in this case on October 3, 2003 expressly acknowledges on the record that the currently claimed subject matter is fully patentable and not rendered obvious by either such teaching, even if it assumed this subject matter is present in the prior art, which Applicants do not concede. In particular, the Restriction Requirement states that “the invention of Groups I-XXVI are each capable of being separately made, independently used *and the patentability of one would not render the other obvious or unpatentable.*” Restriction Requirement at. p. 4, 3rd ¶ (emphasis added). The first four claim

groupings set for by the Restriction Requirement are as follows:

- i. Claims 1, 2, 4-10, are drawn to plants and seeds that are resistant to at least two herbicides, classified in class 800, subclass 312.
- ii. Claims 12-20 are drawn to soybean plants and seeds that are resistant to at least two herbicides, classified in class 800, subclass 312.
- iii. Claims 11, 21 are drawn to a soybean seed that is resistant to ALS inhibitor and glufosinate herbicides, classified in class 800, subclass 312.
- iv. Claims 11, 22 are drawn to a soybean seed that is resistant to glyphosate and glufosinate herbicides, classified in class 800, subclass 312.

The Restriction Requirement therefore expressly acknowledges that the currently elected subject matter, which corresponds to the Group IV claims, is ***not rendered obvious or unpatentable*** by any of: (a) “plants and seeds that are resistant to at least two herbicides”, (b) “soybean plants and seeds that are resistant to at least two herbicides”, or (c) “soybean plants and seeds that are resistant to ALS inhibitor and glufosinate herbicides.” The Office therefore cannot now assert precisely the opposite, as has been done based on the citation to the Rhodes reference. The claims are therefore patentable over the prior art for at least this additional reason.

3. Botterman *et al.* Does Not Teach Transgenic Glufosinate-Tolerant Soybean Plants

The Action additionally states that Botterman *et al.* teach soybean plants resistant to glufosinate, and the resistant or tolerant phenotype has shown commercially acceptable grain yield. In response, Applicants note that, while this reference does refer to glufosinate tolerance for other species such as tobacco, sugar beets, and alfalfa, it does ***not*** teach transgenic glufosinate-tolerant soybean plants with commercially acceptable grain yield.

Specifically, Botterman notes that “***observations in the laboratory . . . have to be followed by open field trials to prove a statistically significant performance and to provide***

yield data” (p. 358, emphasis added). While the reference refers to field tests of other plants with glufosinate-tolerance, such as tobacco, sugar beets, and alfalfa, it does not show field tests for a soybean plant. Due to the complexity of the effects of a given modification as previously explained in the Declaration of Dr. Joseph R. Byrum submitted with Applicants’ previous response, results relating to field tests of other species would not be applicable to soybean plants. In fact, Botterman expressly notes the importance of field testing each species, stating that “tobacco lines containing these chimeric genes generally were fully resistant, [but] it was observed that alfalfa lines gave *different results*” (p. 360, emphasis added). Without field tests specifically for the soybean, the results from producing the soybean plant with this trait are speculative and unpredictable, even setting aside the issue of what would happen were a second transgene introduced. This is underscored by the evidence entered in the record with Applicants’ previous Response, which is further discussed below, demonstrating that those of skill in the art as of the filing date would have been aware of multiple contemporaneous reports associating glyphosate tolerance genes with a yield *loss*.

4. The First and Second Byrum Declarations Establish Non-Obviousness

The absence of the Rhodes patent as prior art and the lack of teaching of soybean plants resistant to glufosinate by Botterman more than fully demonstrate the non-obviousness of the claimed invention alone. In addition, Applicants have further demonstrated the non-obviousness of the invention by way of the First and Second Byrum Declarations.

As stated in the Declaration of Dr. Joseph R. Byrum submitted previously, a soybean variety had never been developed prior to the invention having more than one herbicide resistance transgene combined in a single soybean plant. It was also explained that the expression of herbicide resistance transgenes requires manipulation of complex metabolic

pathways of plant cells. As soybean plants do not naturally exhibit herbicide tolerance, the results of a given modification are unpredictable.

The current Action nonetheless asserted that this information was not persuasive, stating that Rhodes teaches soybean seeds and plants that have resistance to glyphosate and contain the ALS gene for sulfonylurea tolerance, demonstrating successful gene stacking. As noted above, however, Rhodes is not prior art and in fact represents work carried out on behalf of the current Assignee.

Dr. Byrum also explains that transgene expression causes complex pleiotropic effects that may or may not be detectable at the phenotypic level. The effects can vary depending upon factors that include location of insertion of the transgene, the type of transgene being expressed, the genotype of the host soybean plant, and the regulatory elements and any enhancers used to express the transgene. It was further explained that the expression of enzymes not normally present in the plants creates a “metabolic drag” reducing energy from the diversion of resources to the expression of the transgene. Combined with the uncertainty of potential interactions among interrelated metabolic pathways, including negative or positive feedback regulation of different pathways from altered substrate or precursor production, the difficulties are not merely additive when combining multiple herbicide resistance transgenes, but rather are exponential. For example, it was noted that metabolic drag and/or pleiotropic effects associated with transgene expression could have been expected to limit the availability of necessary substrates in the metabolic pathways. It was noted in this regard that certain traits are known to be negatively correlated, such as protein and oil. Dr. Byrum therefore concluded that one of skill in the art simply would have had no reasonable expectation of success as of the priority date that

transgenes conferring tolerance to glyphosate and glufosinate could both be properly expressed to obtain the requisite herbicide tolerance.

Therefore, one of ordinary skill in the art would not have reasonably predicted as of the filing date that a plant could be obtained comprising transgenes conferring tolerance to glyphosate and glufosinate and also having commercially significant yield. Whether this is true today is completely irrelevant for purposes of the §103 analysis, as whether an art is predictable or whether a proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. See MPEP § 2143.02, *citing Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986). In this case, it was an open question in the art as of the priority date whether a single transgene could be expressed without deleteriously impacting yield, let alone two such genes.

The Action finds this unpersuasive, stating that the Rhodes patent found the cultivar had shown uniformity and stability for relevant traits. Once again, however, the Rhodes patent is not prior art. The Action also notes that Botterman states that the strategy for plant engineering set forth in the reference is highly effective and has no effect on crop performance. However, Botterman deals with a single transgene and expressly acknowledges that field trials were not carried out, and thus no teaching is provided regarding whether a commercially acceptable yield could be obtained even for one transgene. Given the highly complex nature of the interactions caused by expression of the transgenes as explained by Dr. Byrum, results from field tests of species such as tobacco, sugar beets and alfalfa would not be applicable to the current case. Additionally, as the difficulties are not merely additive when combining multiple herbicide resistance transgenes but rather are exponential, field tests done with only one transgene expressed would also not be relevant to predicting the likelihood of success of expressing two

transgenes while retaining commercially significant yield. Therefore, as of the priority date, it remained an open question in the art whether even a single herbicide tolerance transgene could be expressed without deleteriously impacting yield, let alone two such genes.

One of ordinary skill in the art therefore would have also been without any motivation to try to arrive at the invention. As explained in the specification, yield is routinely considered the highest priority by most soybean breeders. In fact, Oplinger *et al.*, 1999 (www.biotech-info.net/soybean_performance.pdf) asserted that a 4% yield loss allegedly due to the presence of a glyphosate tolerance gene in RR soybeans would represent a loss to farmers of approximately \$1 billion per year if averaged across the entire U.S. soybean crop. While applicants do not agree with the 4% loss figure based on the information available today, this is evidence of the importance placed on yield in soybeans and of the general expectations in the art as of the priority date against which obviousness must be viewed. The allegations of a yield loss for a single transgene would only be expected to be compounded in the case of two such transgenes. One of ordinary skill in the art as of the filing date would therefore have been taught away from attempting to stack multiple herbicide tolerance transgenes, and would not have reasonably believed a commercially significant yield could be obtained when doing so. This additionally fully establishes the non-obviousness of the claims.

5. Summary

In sum, Applicants have demonstrated that the Rhodes patent may not be used as prior art against the current case, and that Botterman does not teach transgenic glufosinate-tolerant soybean plants. The patentable distinctiveness of the current invention over the cited art was further already acknowledged on the record in the Restriction Requirement mailed October 3, 2003. Additionally, Applicants have presented substantial evidence demonstrating that, as of the

priority date, one of skill in the art would not have had a motivation or reasonable expectation of success in producing a soybean plant comprising transgenes conferring glyphosate and glufosinate tolerance and having a commercially significant yield, both from the standpoint of herbicide tolerance and yield. Applicants reiterate that regardless of the description of soybean plants resistant to glyphosate or glufosinate alone, the fact remains that prior to the invention one of skill in the art would not have known how multiple herbicide tolerance genes would interact. This is underscored, as shown by declaratory evidence on the record, by the unpredictable and synergistic effects observed when herbicides are combined, the complex biochemical pathways that must be modified to obtain herbicide tolerance, the state of teaching in the art and the unpredictable and non-additive manner in which genes interact in plants as noted in the specification and Declaration of Joseph Byrum. The Second Declaration of Joseph Byrum further demonstrates that, as of the priority date, one of skill in the art would have had no clear motivation to combine such transgenes, and no reasonable expectation that such a combination would lead to a desirable result from the standpoint of seed yield.

Applicants therefore respectfully submit that nonobviousness has been fully established on the record by substantial evidence and that no evidence has been presented for doubting this showing. Removal of the rejection under 35 U.S.C. § 103 is thus respectfully requested.

C. Request for Timely Prosecution of the Case

Applicants respectfully note that this is the fifth non-final Office Action received in the case. No adequate basis for rejecting the case has been presented to date and Applicants have fully demonstrated herein and in the previous responses that no such basis exists. The delay in prosecution serves no statutory basis in the Patent Laws and is contrary to MPEP §§707.02 and

707.07, which caution against piecemeal examination. Advancement of the prosecution of the case in a timely manner is thus respectfully requested.

D. Conclusion

In light of the foregoing, applicants submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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